REMARKS

1. AMENDMENTS

1.1 Claims

Claims 96-107 and 110-155 were pending. The Examiner states that claims 118, 119, 124, 125, 129-131, 133 and 135 are allowed (Office Action at p. 26). Claim 128 has been cancelled without prejudice. Applicants reserve the right to pursue the cancelled or removed subject matter in the instant application or in one or more related applications.

Claims 96, 97, 99, 102, 103, 106, 107, 116, 117, 129, and 138, have been amended to clarify that which Applicants regard as the invention. In particular, claims 96, 97, 102, 103, 116, and 117 have been amended to recite "monoclonal antibody." Support for this amendment can be found in the specification as filed, for example, at p. 3, ¶ [0010]; p. 9, ¶ [0060]; and p. 15, ¶ [0083].

Claims 96, 97, 102, 103, 116, and 117 have been amended to specify that the antibody "specifically" binds to human IL-13. Support for this amendment can be found in the specification as filed, for example, at p. 3, ¶ [0010]; p. 49, ¶¶ [00233]-[00235]; and p. 37, ¶¶ [00183]-[00184].

Claims 102 and 103 have been amended to indicate the correlation between the CDR amino acid sequences of SEQ ID NOs: 99, 104, 115, 117, 123, and 135 and the other CDR amino acid sequences referenced by sequence identification numbers in the claims. Support for this amendment can be found in the specification as filed, for example, at pp. 45-49, ¶¶ [00222]-[00232]; and Figures 15, 17, and 20.

Claims 106, 107, and 129 have been amended to list the type of antibodies in the alternative instead of in a Markush group.

Claims 99 and 138 have been amended to correct inadvertent and obvious typographical/clerical errors.

Accordingly, no new matter is introduced by these amendments. Upon entry of this Amendment, claims 96-107, 110-127, and 129-155 will be pending in the instant application, and claims 118, 119, 124, 125, 129-131, 133 and 135 are allowed.

1.2 Specification

The specification has been amended as follows in view of the objections raised in the Office Action:

- Paragraph [0038] at page 7 has been amended to reference and to describe all the portions of Figure 11, *i.e.*, Figures 11A-1, 11A-2, 11B-1, 11B-2, 11C-1, 11C-2, 11D-1, and 11D-2;
- Paragraph [0039] at page 7 has been amended to reference and to describe all the portions of Figure 12, *i.e.*, Figures 12A-1, 12A-2, 12B-1, 12B-2, 12C-1, 12C-2, 12C-3, 12C-4, 12D-1, 12D-2, 12D-3, and 12D-4.
- Paragraph [0040] at page 7 has been amended to delete reference to Figure 13E, which is not present;
- Paragraph [0045] at page 7 has been amended to recite the sequence identification numbers for the amino acid sequences depicted in Figure 18;
- Paragraph [0046] at page 7 has been amended to recite the sequence identification numbers for the amino acid sequences depicted in Figure 19;
- Paragraph [0048] at page 7 has been amended to reference and to describe all the portions of Figure 21, *i.e.*, Figures 21A and 21B; and
- Paragraph [00218] starting at page 43 has been amended to delete reference to Figure 13E, which is not present.

Accordingly, no new matter is introduced by these amendments.

1.3 Substitute Sequence Listing

In response to the Notice, the specification has been amended by replacing the Sequence Listing of record with the Substitute Sequence Listing submitted concurrently herewith, in paper and computer-readable format (CRF). In particular, the Substitute Sequence Listing submitted herewith has been amended to include new SEQ ID NOs: 153-193 for amino acid sequences depicted in Figures 11A-1 to 11D-2, 12A-1 to 12D-4, 15, 18 and 19. Support for these amendments can be found in the application as filed, for example, Figures 11A-D, 12A-D, 15, 18, and 19. Accordingly, no new matter is introduced by these amendments.

1.4 Drawings

Figures 11A-D, 12A-D, and 15 have been amended to include sequence identification numbers for the amino acid sequences depicted therein. Specifically, each of Figures 11A-D and 12A-D, which was originally on one sheet, has been split up to fit onto two or more sheets due to the larger size. Accordingly, Figure 11A is now labeled Figure 11A-1 and 11A-2; Figure 11B is now labeled Figure 11B-1 and 11B-2; Figure 11C is now labeled Figure 11C-1 and 11C-2; Figure 11D is now labeled Figure 11D-1 and 11D-2; Figure 12A is now labeled 12A-1 and 12A-2; Figure 12B is now labeled 12B-1 and 12B-2; Figure 12C is now labeled Figure 12C-1, 12C-2, 12C-3 and 12C-4; and Figure 12D is now labeled Figure 12D-1, 12D-2, 12D-3, and 12D-4.

In addition, the following amendments were made to Figures 11 and 12:

1. For all portions of Figures 11 and 12, a column for the names of the clones as depicted in original Figures 11A, 11C, 12A and 12C, have been added to the left of the table where appropriate for clarity;
2. The following labels in Figures 11A-D and 12A-D have been rotated 90 degrees counterclockwise: CDR1, CDR2, and CDR3;
3. For all portions of Figures 11 and 12, a column under the label "SEQ ID NO" separate from the column under the label "CDR1", "CDR2", or "CDR3" was added for including sequence identification numbers for the framework region sequences depicted;
4. In Figures 11A and 11C, "FM1" is replaced with "FR1" for framework region 1; and "FM2" is replaced with "FR2" for framework region 2 to correct typographical errors; and
5. In Figures 11B and 11D, "FM3" is replaced with "FR3" for framework region 3; and "FM4" is replaced with "FR4" for framework region 4 to correct typographical errors.

Figure 15 has been amended by including sequence identification numbers for the amino acid sequences depicted.

Accordingly, no new matter is introduced by these amendments.

2. REJECTIONS UNDER 35 U.S.C. § 112, 1ST ¶, ENABLEMENT

2.1 Overbreadth

Claims 96-107, 110-117, 120-123, 126-128, 132, 134 and 136-155 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement commensurate with the scope of these claims (Office Action at pp. 9-20).

In this regard, the Examiner *admits* that the specification *is* "enabling for making an using a polynucleotide encoding a heavy chain or a variable heavy chain region of an antibody that specifically binds to human interleukin-13 (IL-13) and a polynucleotide encoding a light chain or a variable light chain region of an antibody that specifically binds to human interleukin-13 (IL-13), wherein said antibody comprises a light chain variable region comprising complementarity determining regions (CDRs) having the amino acid sequences of SEQ ID NO: 99, SEQ ID NO: 104, and SEQ ID NO: 115 and a heavy chain variable region comprising CDRs having the amino acid sequences of SEQ ID NO: 117, SEQ ID NO: 123, and SEQ ID NO: 135" (Office Action at pp. 9-10). However, the Examiner contends that (1) only a nucleic acid molecule encoding a portion of an anti-IL-13 *monoclonal* antibody is enabled; (2) only monoclonal antibodies with the *full set of six CDRs* having the amino acid sequences of SEQ ID NOs: 99, 104, 115, 117, 123, and 135 are enabled; (3) the specification does not enable "antigen-binding regions" derived from an anti-IL-13 antibody comprising the amino acid sequence of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657; and (4) the specification does not enable "a humanized antibody of the antibody produced by a hybridoma" designated with ATCC accession number PTA-5657. Applicants disagree for the reasons set forth below.

Legal Standard

The test for enablement is whether one reasonably skilled in the pertinent art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue:

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, ... then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.

In re Angstadt, 190 USPQ 214 (CCPA 1976), at 219.

Thus, all that is required is a reasonable amount of guidance with respect to the direction of the experimentation; reasonable certainty with regard to the outcome of the experimentation is not required.

The Board of Patent Appeals and Interferences ("Board") has applied the principles of *Angstadt* to a biotechnological context. *In re Neuberger & Rabbitts*, 2002 WL 33952578 (B.P.A.I. 2002). The rejected claims in *Neuberger* were directed to chimeric antibodies with (i) a certain antigen binding activity; and (ii) a certain biological activity. The Examiner in *Neuberger* had rejected these claims based on lack of predictability. The Board reversed the Examiner's decision because "a requirement for certainty would be incompatible with any amount of experimentation and therefore incompatible with the standard of enablement." *Id.* at 3.

Monoclonal Antibodies

With respect to rejected claims 96-107, 110-117, 120-123, 126-128, 132, 134 and 136-155, the Examiner contends that the specification is enabling for a polynucleotide encoding a portion (*e.g.*, a heavy chain, a variable heavy chain region, a light chain, or a variable light chain region) of a *monoclonal* antibody, but not all antibodies, such as a polyclonal antibody (Office Action at p. 11). Solely in order to expedite prosecution, and without conceding to the propriety of the rejection, independent claims 96, 97, 102, 103, 116, and 117 have been amended to recite "monoclonal antibody" which includes "a chimeric antibody, or a humanized antibody" (see the instant application at p. 3, ¶ [0010]).

Full Set of Six CDRs

The Examiner states that the specification is enabling for a polynucleotide encoding a portion (*e.g.*, a heavy chain, a variable heavy chain region, a light chain, or a variable light chain region) of an antibody that specifically binds to human IL-13 comprising a full set of six CDRs having the amino acid sequences of SEQ ID NOs: 99, 104, 115, 117, 123, and 135, but not of an antibody which may contain substitutions, deletions and insertions within such six CDRs (Office Action at pp. 12 and 17-18).

Claims 100, 101, 102, 103, 14, 105, 110, and 111 recite the amino acid sequence of only one of the two variable chain regions, or of only the three CDRs of one variable chain region of an antibody. With respect to these claims, and claims which depend therefrom, Applicants submit that the claimed polynucleotides encoding such antibodies are enabled by recitation of the amino acid sequence of only one of the two variable chain regions, or of only the three CDRs of one variable chain region of an antibody, because one of skill in the art could readily select additional CDRs using routine methods known in the art as of the filing date of the instant application. Chain shuffling by panning a light- or heavy-chain library, for example, was a well-established technique for selecting the second complementing antibody chain for constructing humanized antibodies (*see, e.g.*, p. 12, ¶ [0070] of the instant application). For example, Rader *et al.*, 1998, Proc. Natl. Acad. Sci. USA 95:8910-8915 ("Rader," submitted herewith as reference C134 with the Supplemental Information Disclosure Statement filed concurrently herewith), teaches the humanization of the mouse anti-$\alpha v\beta 3$ antibody by identifying a complementing light chain or heavy chain, respectively, from a human light chain or heavy chain library. The

resultant humanized antibody variants had affinities as high or higher than the affinity of the original antibody.

Thus, methods for producing antibodies with specificity for a particular antigen by combining three CDRs from an antibody specific for the antigen with other unknown CDRs, *e.g.*, from a heavy chain or light chain library, were routine in the art as of the filing date of the instant application. Accordingly, the skilled artisan could make and use the polynucleotides of claims 100, 101, 102, 103, 14, 105, 110, and 111, and claims which depend therefrom, without any undue experimentation.

Antigen-Binding Regions

With respect to claims 96 and 97, the Office Action states that the specification is not enabling for "antigen-binding regions" *derived from* an anti-IL-13 antibody comprising the amino acid sequence of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657, because the term "antigen-binding regions" allegedly is not defined with any of the requisite clarity and particularity to permit the skilled artisan to immediately envision its structure and thus requiring undue and unreasonable experimentation (Office Action at p. 12). Applicants disagree for the reason set forth below.

The specification does enable "antigen-binding regions" *derived from* the 228B/C-1 antibody (*i.e.*, antibody produced by hybridoma designated with ATCC accession number PTA-5657). First, the specification describes "antigen-binding regions" in great detail. For example, the specification discloses that antigen-binding fragments may include Fab, Fab', F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and single domain antibodies comprising either a VL or VH domain, as well as single-chain antibodies comprising the variable region(s) alone or in combination with the entirety or a portion of a hinge region, CH1, CH2, and/or CH3 domains (*see* the instant application, *e.g.*, at p. 4, ¶ [0013]; p. 15, ¶ [0085]). Also described are IL-13-binding fragments comprising CDRs (see the instant application at p. 4, ¶ [0012]; p. 20, ¶¶ [00106] and [00108]). Methods of making such antigen-binding fragments are also disclosed in the specification (*see* the instant application, *e.g.*, at p. 21, ¶ [00110]; p. 19, ¶ [00102]; p. 20, ¶ [00106]).The specification also provides an example of an antigen-binding fragment (*see* the instant specification, *e.g.*, at p. 4, ¶ [0013]; and Figure 21).

Second, the regions of an antibody that are important for antigen-binding are generally known in the art. Therefore, the skilled artisan would recognize that an "antigen-binding region" at the minimum would comprise one or more CDRs of an antibody, and would comprise sufficient amino acid sequences within the light chain and heavy chain variable regions to allow for specific binding to human IL-13.

In the instant case, the skilled artisan could readily make and use "antigen-binding regions" derived from an anti-IL-13 antibody comprising the amino acid sequence of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657, because the instant application discloses the amino acid sequences of the variable regions of the 228B/C-1 antibody (*i.e.*, the antibody produced by the hybridoma designated with ATCC accession number PTA-5657), and the sequences of the CDRs therein which are important for specific binding to human IL-13. In view of such information, the skilled artisan could readily envision the structure of an antigen-binding region derived from the amino acid sequence of the 228B/C-1 antibody, and would only have to perform routine experimentation to confirm the binding specificity to human IL-13 of an antigen-binding region derived from the amino acid sequence of the 228B/C-1 antibody. No undue experimentation is required.

Humanized Antibodies

With respect to claims 116 and 117 relating to a polynucleotide encoding a portion of a "humanized" antibody of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657, and claims which depend therefrom, the Examiner acknowledges that the level of skill in the art is relatively high, and it may be well within the skill of the artisan to graft the three CDRs from both the light and heavy chain variable regions of the disclosed antibody into the framework of a human antibody without substantial loss of affinity and specificity (Office Action at pp. 17-18). However, the Examiner notes that the claims are not limited to polynucleotides encoding portions of such engineered antibodies (Office Action at pp. 17-18). In particular, the Examiner contends that if any one or more of the full six CDRs of the 228B/C-1 antibody (*i.e.*, antibody produced by a hybridoma designated with ATCC accession number PTA-5657) is omitted from a humanized antibody, then the consequences upon antigen binding specificity are unpredictable.

Applicants submit that the specification is enabling for the claimed polynucleotide encoding a portion (*e.g.*, light chain, light chain variable region, heavy chain, or heavy chain variable region) of a "humanized" antibody of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657. First, as discussed above, the specification is enabling for a polynucleotide encoding a heavy chain, a variable heavy chain region, a light chain, or a variable light chain region of an antibody that specifically binds to human IL-13 comprising less than the full set of six CDRs, for example the three light chain CDRs or the three heavy chain CDRs.

Second, the specification describes how to make and use humanized antibodies of the 228B/C-1 antibody, wherein the humanized antibodies comprises the full set of six CDRs, as well as humanized antibodies comprising variations in one or more of the full set of six CDRs due to CDR optimization. For example, the specification describes the important features of humanized antibodies and methods of generating the same, such as CDRs and ability to bind to IL-13 (see the instant application, *e.g.*, at p. 12, ¶ ¶ [0070]-[0071]; p. 20, ¶ [00106]). Moreover, the specification provides working examples relating to the generation of a series of humanized antibodies of the 228B/C-1 antibody (produced by hybridoma having ATCC accession no. PTA-5657), including antibodies containing optimized CDRs (see the instant application at pp. 40-49, Examples 9 and 10). The antibodies containing optimized CDRs would be considered to contain less than the full six CDRs of the 228B/C-1 antibody, because one or more of the CDR sequences have been altered while maintaining binding specificity to human IL-13. Therefore, generation of the humanized antibodies derived from the 228B/C-1 antibody disclosed in the specification provides guidance and enabling disclosures for the skilled artisan, both with respect to the structure and function of the genus of humanized antibodies of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657 as specified in claims 116 and 117.

Moreover, as taught in the instant specification, binding assays and competition assays are well known and routine assays that the skilled artisan can readily perform to confirm the binding specificity to human IL-13 of the humanized antibodies recited in claims 116 and 117. Therefore, undue experimentation would not be required to make and used the humanized antibodies recited in claims 116 and 117.

In view of the foregoing, the rejection of claims 96-107, 110-117, 120-123, 126-128, 132, 134 and 136-155 under 35 U.S.C. § 112, first paragraph, for lack of enablement, should be withdrawn, because the claims are enabled.

2.2 Declaration Regarding Deposited Microorganism under the Budapest Treaty

Claims 96-107, 110-117, 120-123, 126-128, 132, 134 and 136-155 are directed to a polynucleotide encoding a portion (*e.g.*, light chain, light chain variable region, heavy chain, or heavy chain variable region) of an antibody derived from an antibody produced by the hybridoma cell line (accession number PTA-5657) deposited with the American Type Culture Collection under the provisions of the Budapest Treaty. The Office Action requests the filing of an affidavit or declaration, signed by the applicant, assignee or an attorney of record having authority and control over the deposit, stating that all restrictions on public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced should it become nonviable or be destroyed during the effective term of the deposit.

In order to expedite prosecution of the instant application, and without conceding to the propriety of the rejection, Applicants submit herewith a Statement Regarding the Permanence and Availability of Deposited Microorganisms under 37 C.F.R. §§ 1.801-1.809 by Irene T. Pleasure, Head of Patents of Genentech, Inc. regarding the deposit PTA-5657, pursuant to the Office Action's request. Accordingly, the rejection should be withdrawn.

3. REJECTIONS UNDER 35 U.S.C. § 112, 1ST ¶, WRITTEN DESCRIPTION

Claims 96-107, 110-117, 120-123, 126-128, 132, 134 and 136-155 are rejected under 35 U.S.C. § 112, first paragraph for lack of written description (Office Action at pp. 20-26). In this regard, the Examiner *admits* that the instant disclosure "would only reasonably convey Applicant's possession as of the filing date of this application of a polynucleotide encoding a heavy chain or a variable heavy chain region of an antibody that specifically binds to human Interleukin-13 (IL-13) and a polynucleotide encoding a light chain or a variable light chain region of an antibody that specifically binds to human Interleukin-13 (IL-13), wherein said

antibody comprises a light chain variable region comprising complementarity determining regions (CDRs) having the amino acid sequences of SEQ ID NO: 99, SEQ ID NO: 104, and SEQ ID NO: 115 and a heavy chain variable region comprising CDRs having the amino acid seqeuences of SEQ ID NO: 117, SEQ ID NO: 123, and SEQ ID NO: 135" (Office Action at pp. 22-23). However, the Examiner contends that the instant application would not reasonably convey to the skilled artisan that Applicant had possession of the genus of antibodies, including both monoclonal and polyclonal antibodies having substantially disparate structures (*e.g.*, having CDRs that vary substantially, relative to the amino acid sequences disclosed), or of the claimed genus of a plurality of polynucleotides encoding polypeptides comprising particular portions of such genus of antibodies (Office Action at pp. 22-23). The Examiner also contends that there is no language that adequately describes with the requisite clarity and particularity at least a substantial number of the numbers of the claimed genus of antibodies having such widely varying structures which have the ability to bind a human IL-13 polypeptide (Office Action at p. 23). Applicants disagree for the reasons set forth below.

Legal Standard

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See, e.g., Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

The factors used for evaluating the adequacy of the disclosure for generic claims include the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science and technology, and the predictability of the aspect at issue. *See Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005) (holding that when the prior art discloses the sequences for nucleotides, the specification need not reiterate the known sequence information to meet the written description requirement for claimed genus of chimeric genes), *cited with approval in Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, No. 598 F.3d 1336 (Fed. Cir. 2010). S*ee also Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006) (holding that where accessible literature sources provided relevant nucleotide sequence information, satisfaction of the written description

requirement does not require recitation or incorporation by reference of the sequences in the specification).

The Claims Have Written Description Support

Claim 96 as amended is directed to a polynucleotide encoding a heavy chain or a variable heavy chain region of a *monoclonal* antibody that specifically binds human IL-13, wherein said antibody comprises antigen-binding regions derived from an anti-IL-13 antibody comprising the amino acid sequence of an antibody produced by a hybridoma designated with American Type Culture Collection ("ATCC") accession number PTA-5657.

Claim 97 as amended is directed to a polynucleotide encoding a light chain or a variable light chain region of a *monoclonal* antibody that specifically binds human IL-13, wherein said antibody comprises antigen-binding regions derived from an anti-IL-13 antibody comprising the amino acid sequence of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657.

Claim 116 as amended is directed to a polynucleotide encoding a heavy chain or a variable heavy chain region of a *monoclonal* antibody that specifically binds human IL-13, wherein said antibody is a humanized antibody of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657.

Claim 117 as amended is directed to a polynucleotide encoding a light chain or a variable light chain region of a *monoclonal* antibody that specifically binds human IL-13, wherein said antibody is a humanized antibody of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657.

Applicants submit that the specification provides written description support for the monoclonal antibodies specified in the claims. The specification describes a combination of structural features (*e.g.*, heavy chain and light chain variable regions, CDRs, optimized CDRs) and functional features (*e.g.*, specifically binding to human IL-13) representative of the monoclonal antibodies specified in the claims, and provides working examples of such monoclonal antibodies, *e.g.*, murine antibody, chimeric antibody, and humanized antibodies of the 228B/C-1 antibody. Moreover, the specification also describes humanized antibodies of the 228B/C-1 antibody comprising amino acid substitutions in their CDRs to generate optimized CDRs (*see* Example 10 of the instant application). Such humanized antibodies comprise less

than the full set of six CDRs of 228B/C-1, because the original CDRs have been modified to generate optimized CDRs.

Therefore, contrary to the Examiner's contention, the specification describes numerous species of monoclonal antibodies, including chimeric antibodies and humanized antibodies, representative of the genus of monoclonal antibodies specified in the claims, and the structures common to the species within the genus. Specifically, the instant specification disclose that (i) from 5200 candidate humanized antibodies of the 228B/C-1 antibody screened, 300 candidates yielded binding results comparable to the chimeric clone (see p. 42, ¶ [00213]; pp. 40-44, Example 9; Figures 11 and 12); and (ii) to generate humanized antibodies comprising optimized CDRs, over 1100 candidates were screen using functional ELISA assay and a total of 120 candidates were identified as having activity greater than the parent clone (see pp. 45-49, Example 10; Figure 15; and Figure 17). Applicants submit that the hundreds of monoclonal antibodies described in the specification, in particular, humanized antibodies of 228B/C-1 and affinity matured humanized antibodies of 228B/C-1, provide more than an adequate number of species within the genus of monoclonal antibodies specified in the claims. The numerous species of monoclonal antibodies, including chimeric and humanized antibodies, described in the specification clearly convey to a skilled artisan that the inventor was in possession of the claimed invention at the time the application was filed.

Thus, the specification provides sufficient written description support of polynucleotides encoding particular portions (*e.g.*, heavy chain, variable heavy chain region, light chain, or variable light chain region) of the monoclonal antibodies, including chimeric and humanized antibodies, specified in the claims to meet the written description requirement.

In view of the foregoing, the rejection of claims 96-107, 110-117, 120-123, 126-128, 132, 134 and 136-155 under 35 U.S.C. § 112, first paragraph, for lack of written description should be withdrawn.

4. REJECTIONS UNDER 35 U.S.C. § 112, 2ND ¶, INDEFINITENESS

Claims 116, 117, 126-128, 132 and 138-155 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention (Office Action at pp. 7-8). In particular, with respect to claims 116 and 117 drawn to "a humanized antibody of an antibody produced by a hybridoma", the Office Action states that it cannot be ascertained what structural properties need be attributed to the claimed antibody such that it is dubbed "a humanized antibody of an antibody produced by a hybridoma. Applicants disagree for the reasons set forth below.

The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986).

Applicants submit that those skilled in the art would understand and would be able to ascertain the important properties attributed to the humanized antibodies specified in claims 116 and 117, and claims 126-128, 132 and 138-155, which depend therefrom, when the claims are read in light of the specification. In particular, the specification describes the important features of humanized antibodies and methods of generating the same, such as CDRs and ability to bind to IL-13 (see the instant application at p. 12, ¶¶ [0070]-[0071]; p. 20, ¶¶ [00106]). Moreover, the specification provides working examples relating to the generation of numerous humanized antibodies derived from the 228B/C-1 antibody (produced by hybridoma having ATCC accession no. PTA-5657), including antibodies containing optimized CDRs (see the instant application at pp. 40-49, Examples 9 and 10, Figures 15, 17, and 21). The humanized antibodies generated from the 228B/C-1 antibody provide guidance to those skilled in the art in ascertaining the structural properties (*e.g.*, CDR amino acid sequences), as well as functional properties (*e.g.*, specific binding to human IL-13), attributed to the humanized antibody of an antibody produced by a hybridoma designated with ATCC accession number PTA-5657 as specified in claims 116 and 117. Therefore, claims 116 and 117, and claims 126-128, 132 and 138-155, which depend therefrom, are clear and definite with respect to the recited humanized antibody.

Accordingly, the rejection of claims 116, 117, 126-128, 132 and 138-155 under 35 U.S.C. § 112, second paragraph, as being indefinite, should be withdrawn.

5. PRIORITY

The Office Action contends that pending claims 96-107 and 110-155 are not entitled to benefit under §119 and/or §120 to the earlier filing dates of the priority document claimed, since these claims stand rejected under 35 U.S.C. §112, first paragraph as lacking adequate written description and/or a sufficiently enabling disclosure. Accordingly, the effective filing date of these claims is deemed to be the filing date of international application PCT/US04/43501, namely December 23, 2004.

First, the amended claims obviate the rejections under 35 U.S.C. §112, first paragraph.

Second, Applicants submit that the instant claims are entitled to benefit under 35 U.S.C. §119(e) from the earlier filing date of December 23, 2003 of U.S. Provisional Application No. 60/532,130 ("the Provisional Application"), because the Provisional Application has written description support and enabling disclosure for the instant claims as amended. For example, the Provisional Application discloses the 228B/C-1 antibody, the deposited hybridoma which produces such antibody, and the three light chain variable region complementarity determining regions (CDRs) as well as the three heavy chain variable region CDRs (see the Provisional Application at p. 4, ¶ [0011]; p. 8; and Figure 8). The Provisional Application also discloses monoclonal antibodies, humanized antibodies, human antibodies, chimeric antibodies, Fab fragments, and F(ab') fragments (see the Provisional Application at ¶¶ [0066]-[0068]). The Provisional Application also describes methods of making such antibodies. Therefore, one of skill in the art could readily make and use the monoclonal antibodies derived from the 228B/C-1 antibody as specified in the claims, based on the disclosure of the Provisional Application. Accordingly, the instant claims as amended are entitled to benefit under 35 U.S.C. §119(e) from the earlier filing date of December 23, 2003 of the Provisional Application, and at the minimum, the instant claims are entitled to the filing date of December 23, 2004 which is the filing dateof international application PCT/US04/43501, of which the instant application is a national stage.

In view of the foregoing, Applicants request the Examiner's reconsideration of the effective filing date of the instant claims and the effective filing date of the instant application.

6. OBJECTIONS TO THE CLAIMS

Claims 102 and 103 are objected to, as being drawn in the alternative to the subject matter of non-elected species of the invention (Office Action at p. 6). In the Office Action mailed October 13, 2010, the Examiner stated that "[u]pon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise require all the limitations of an allowed generic claim" (see p. 5 of Office Action mailed October 13, 2010). See also, 37 C.F.R. § 1.141.

As amended, claims 102 and 103 have been redrafted as generic independent claims. The species of CDR sequences specified in claims 102 and 103 are linked in that they are the elected CDR species or a variation of the elected CDR species consisting of one or two amino acid sequence substitutions to generate optimized CDR sequences (see the instant application at pp. 45-49, Example 10; Figures 15-17 and 20). Therefore, the objection is obviated.

Claim 99, 107, 113, 115, 136, and 137 are objected to because claim 99 uses "(ii)" twice (Office Action at p. 6). The objection is overcome, because claim 99 has been amended to correct the clerical error.

Claims 98, 100, 101, 104-105, 110, 111 and 120-123 are rejected as being specifically directed to a deposited material wherein it is alleged that the specification provides insufficient assurance that all required deposits have been made and the conditions of MPEP § 608.01 have been met so as to satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph (Office Action at p. 6). The Examiner points out that even if this rejection were obviated by the provision of a declaration satisfying these requirements, claims 98, 100, 101, 104-105, 110, 111 and 120-123 would still be objected to as being dependent on a rejected base claim, unless the claims were rewritten in independent form including all of the limitations of the base claim and any intervening claims. In response, Applicants submit that this rejection is overcome, because (i) submitted herewith is a Statement Regarding the Permanence and Availability of Deposited Microorganisms under 37 C.F.R. §§ 1.801-1.809 as required by the Examiner; and (ii) the rejections of claim 96, from which claims 98, 100, 101, 104-105, 110, 111 depend directly or indirectly, is overcome and should be withdrawn in view of the discussions presented above.

Claim 138 is objected to because this claim depends, in error, from claim 18 (rather than from claim 118) (Office Action at p. 7). In response, the objection is obviated by the amendment made herein to correct the inadvertent clerical error.

7. OBJECTIONS TO THE DRAWINGS

The drawings set forth as Figures 11, 12, 15, 18 and 19 are objected to because these figures depict amino acid sequences not identified by sequence identification numbers, either in the drawings or in the brief description of the drawings (Office Action at pp. 4-5). This objection is obviated in view of the submissions presented herein. In particular, Replacement Drawings for Figures 11, 12, and 15 with sequence identification numbers for the amino acid sequences depicted in the respective Figures are submitted herewith. With respect to Figures 18 and 19, the brief description for the respective Figures has been amended to reference sequence identification numbers for the depicted amino acid sequences.

The drawings set forth as Figures 11 (including portions labeled A, B, C, and D), 12 (including portions labeled A, B, C, and D), and 21 (including portions A and B) are objected to because the brief description of these drawings does not provide a description of the separate portions thereof. This objection is obviated in view of the amendments made herein to the specification, specifically to the brief description of the drawings section for such Figures.

8. OBJECTIONS TO THE SPECIFICATION

The specification is objected to because the amino acid sequences depicted in Figures 11, 12, 15, 18 and 19 are not identified, either in the figures or in the brief description of the drawings, by sequence identification numbers as required by 37 C.F.R. § 1.821 (Office Action at pp. 5-6). The objection is obviated in view of the replacement drawings for Figures 11, 12, and 15, the amendments to the brief description for Figures 18 and 19, and the Substitute Sequence Listing, submitted herewith.

The specification is objected to because the brief description of the drawings for Figures 11 and 12 does not provide a description of the separate portions thereof and thus fails to comply

with 37 C.F.R. § 1.84(p)(5) (Office Action at p. 6). The objection is obviated in view of the amendments to the specification made herein.

III. Oath/Declaration

The Office Action states that the declaration is defective because non-initialed and/or non-dated alterations have been made to the document and that a supplemental oath or declaration is required. See 37 C.F.R. 1.52(c) and 37 C.F.R. 1.67(a) (Office Action at p. 3). Applicants believe that this objection is in error. Applicants direct the Examiner's attention to the Declaration (executed in six counterparts) submitted on January 29, 2009. The Declaration does not contain any handwritten alterations. A courtesy copy of the Declaration is submitted herewith. Therefore, the objection to the Declaration should be withdrawn.

9. INFORMATION DISCLOSURE STATEMENT

The Office Action, in error, indicates that the listing of the references cited in the International Search Reports identified as documents C94 and C95 in the Information Disclosure Statement ("IDS") filed December 13, 2010 is not considered to be an IDS complying with 37 C.F.R. § 1.98 , and that the references cited in the International Search Reports have not been considered (Office Action at pp. 2-3).

Applicants take this opportunity to correct the record. Each reference cited in the Search Reports is identified and listed as references A11-A13, C04, and C59, respectively, in the IDS filed September 25, 2009 in compliance with 37 C.F.R. § 1.98. Applicants further note that the Examiner initialed references A10-A12, C04, and C59 indicating that the Examiner has considered these references.

The Search Reports designated as documents C94 and C95 were not submitted as an information disclosure statement under 37 C.F.R. § 1.98, but as "other information" submitted for consideration by the USPTO under 37 C.F.R. § 1.98(a)(1) in an IDS and for completeness of the file.

CONCLUSION

Entry and consideration of the foregoing amendments and remarks is respectfully requested. All rejections of the claims are believed to be overcome or obviated. Withdrawal of all rejections and allowance of the claims is earnestly sought.

It is estimated that no additional fee is necessary for filing this Response. In the event an additional fee is required, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

Date: May 27, 2011

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